



Seizures and Epilepsy: Hope Through Research

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EXHIBIT C

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Introduction

Few experiences match the drama of a convulsive seizure. A person having a severe seizure may cry out, fall to the floor unconscious, twitch or move uncontrollably, drool, or even lose bladder control. Within minutes, the attack is over, and the person regains consciousness but is exhausted and dazed. This is the image most people have when they hear the word epilepsy. However, this type of seizure -- a *generalized tonic-clonic seizure* -- is only one kind of epilepsy. There are many other kinds, each with a different set of symptoms.

Epilepsy was one of the first brain disorders to be described. It was mentioned in ancient Babylon more than 3,000 years ago. The strange behavior caused by some seizures has contributed through the ages to many superstitions and prejudices. The word epilepsy is derived from the Greek word for "attack." People once thought that those with epilepsy were being visited by demons or gods. However, in 400 B.C., the early physician Hippocrates suggested that epilepsy was a disorder of the brain -- and we now know that he was right.

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What is Epilepsy?

Epilepsy is a brain disorder in which clusters of nerve cells, or neurons, in the brain sometimes signal abnormally. Neurons normally generate electrochemical impulses that act on other neurons, glands, and muscles to produce human thoughts, feelings, and actions. In epilepsy, the normal pattern of neuronal activity becomes disturbed, causing strange sensations, emotions, and behavior, or sometimes *convulsions*, muscle spasms, and loss of consciousness. During a seizure, neurons may fire as many as 500 times a second, much faster than normal. In some people, this happens only occasionally; for others, it may happen up to hundreds of times a day.

More than 2 million people in the United States -- about 1 in 100 -- have experienced an unprovoked seizure or been diagnosed with epilepsy. For about 80 percent of those diagnosed with epilepsy, seizures can be controlled with modern medicines and surgical techniques. However, about 25 to 30 percent of people with epilepsy will continue to experience seizures even with the best available treatment. Doctors call this situation *intractable epilepsy*. Having a seizure does not necessarily mean that a person has epilepsy. Only when a person has had two or more seizures is he or she considered to have epilepsy.

Epilepsy is not contagious and is not caused by mental illness or mental retardation. Some people with mental retardation may experience seizures, but seizures do not necessarily mean the person has or will develop mental impairment. Many people with epilepsy have normal or above-average intelligence. Famous people who are known or rumored to have had epilepsy include the Russian writer Dostoyevsky, the philosopher Socrates, the military general Napoleon, and the inventor of dynamite, Alfred Nobel, who established the Nobel Prize. Several Olympic medalists and other athletes also have had epilepsy. Seizures sometimes do cause brain damage, particularly if they are severe. However, most seizures do not seem to have a detrimental effect on the brain. Any changes that do occur are usually subtle, and it is often unclear whether these changes are caused by the seizures themselves or by the underlying problem that caused the seizures.

While epilepsy cannot currently be cured, for some people it does eventually go away. One study found that

children with *idiopathic epilepsy*, or epilepsy with an unknown cause, had a 68 to 92 percent chance of becoming seizure-free by 20 years after their diagnosis. The odds of becoming seizure-free are not as good for adults or for children with severe epilepsy syndromes, but it is nonetheless possible that seizures may decrease or even stop over time. This is more likely if the epilepsy has been well-controlled by medication or if the person has had epilepsy surgery.

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What Causes Epilepsy?

Epilepsy is a disorder with many possible causes. Anything that disturbs the normal pattern of neuron activity -- from illness to brain damage to abnormal brain development -- can lead to seizures.

Epilepsy may develop because of an abnormality in brain wiring, an imbalance of nerve signaling chemicals called *neurotransmitters*, or some combination of these factors. Researchers believe that some people with epilepsy have an abnormally high level of *excitatory neurotransmitters* that increase neuronal activity, while others have an abnormally low level of *inhibitory neurotransmitters* that decrease neuronal activity in the brain. Either situation can result in too much neuronal activity and cause epilepsy. One of the most-studied neurotransmitters that plays a role in epilepsy is *GABA*, or gamma-aminobutyric acid, which is an inhibitory neurotransmitter. Research on GABA has led to drugs that alter the amount of this neurotransmitter in the brain or change how the brain responds to it. Researchers also are studying excitatory neurotransmitters such as glutamate.

In some cases, the brain's attempts to repair itself after a head injury, stroke, or other problem may inadvertently generate abnormal nerve connections that lead to epilepsy. Abnormalities in brain wiring that occur during brain development also may disturb neuronal activity and lead to epilepsy.

Research has shown that the cell membrane that surrounds each neuron plays an important role in epilepsy. Cell membranes are crucial for a neuron to generate electrical impulses. For this reason, researchers are studying details of the membrane structure, how molecules move in and out of membranes, and how the cell nourishes and repairs the membrane. A disruption in any of these processes may lead to epilepsy. Studies in animals have shown that, because the brain continually adapts to changes in stimuli, a small change in neuronal activity, if repeated, may eventually lead to full-blown epilepsy. Researchers are investigating whether this phenomenon, called *kindling*, may also occur in humans.

In some cases, epilepsy may result from changes in non-neuronal brain cells called glia. These cells regulate concentrations of chemicals in the brain that can affect neuronal signaling.

About half of all seizures have no known cause. However, in other cases, the seizures are clearly linked to infection, trauma, or other identifiable problems.

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Genetic Factors

Research suggests that genetic abnormalities may be some of the most important factors contributing to epilepsy. Some types of epilepsy have been traced to an abnormality in a specific gene. Many other types of epilepsy tend to run in families, which suggests that genes influence epilepsy. Some researchers estimate that more than 500 genes could play a role in this disorder. However, it is increasingly clear that, for many forms of epilepsy, genetic abnormalities play only a partial role, perhaps by increasing a person's susceptibility to seizures that are triggered by an environmental factor.

Several types of epilepsy have now been linked to defective genes for *ion channels*, the "gates" that control the flow of ions in and out of cells and regulate neuron signaling. Another gene, which is missing in people with *progressive myoclonus epilepsy*, codes for a protein called cystatin B. This protein regulates enzymes that break down other proteins. Another gene, which is altered in a severe form of epilepsy called *LaFora's disease*, has been linked to a gene that helps to break down carbohydrates.

While abnormal genes sometimes cause epilepsy, they also may influence the disorder in subtler ways. For example, one study showed that many people with epilepsy have an abnormally active version of a gene that increases resistance to drugs. This may help explain why anticonvulsant drugs do not work for some people. Genes also may control other aspects of the body's response to medications and each person's susceptibility to seizures, or *seizure threshold*. Abnormalities in the genes that control neuronal migration -- a critical step in brain development -- can lead to areas of misplaced or abnormally formed neurons, or *dysplasia*, in the brain that can cause epilepsy. In some cases, genes may contribute to development of epilepsy even in people with no family history of the disorder. These people may have a newly developed abnormality, or *mutation*, in an epilepsy-related gene.

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Other Disorders

In many cases, epilepsy develops as a result of brain damage from other disorders. For example, brain tumors, alcoholism, and Alzheimer's disease frequently lead to epilepsy because they alter the normal workings of the brain. Strokes, heart attacks, and other conditions that deprive the brain of oxygen also can cause epilepsy in some cases. About 32 percent of all cases of newly developed epilepsy in elderly people appears to be due to cerebrovascular disease, which reduces the supply of oxygen to brain cells. Meningitis, AIDS, viral encephalitis, and other infectious diseases can lead to epilepsy, as can hydrocephalus -- a condition in which excess fluid builds up in the brain. Epilepsy also can result from intolerance to wheat gluten (also known as *celiac disease*), or from a parasitic infection of the brain called *neurocysticercosis*. Seizures may stop once these disorders are treated successfully. However, the odds of becoming seizure-free after the primary disorder is treated are uncertain and vary depending on the type of disorder, the brain region that is affected, and how much brain damage occurred prior to treatment.

Epilepsy is associated with a variety of developmental and metabolic disorders, including cerebral palsy, neurofibromatosis, pyruvate dependency, tuberous sclerosis, Landau-Kleffner syndrome, and autism. Epilepsy is just one of a set of symptoms commonly found in people with these disorders.

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Head Injury

In some cases, head injury can lead to seizures or epilepsy. Safety measures such as wearing seat belts in cars and using helmets when riding a motorcycle or playing competitive sports can protect people from epilepsy and other problems that result from head injury.

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Prenatal Injury and Developmental Problems

The developing brain is susceptible to many kinds of injury. Maternal infections, poor nutrition, and oxygen deficiencies are just some of the conditions that may take a toll on the brain of a developing baby. These conditions may lead to cerebral palsy, which often is associated with epilepsy, or they may cause epilepsy that is unrelated to any other disorders. About 20 percent of seizures in children are due to cerebral palsy or other neurological abnormalities. Abnormalities in genes that control development also may contribute to epilepsy. Advanced brain imaging has revealed that some cases of epilepsy that occur with no obvious cause may be associated with areas of dysplasia in the brain that probably develop before birth.

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Poisoning

Seizures can result from exposure to lead, carbon monoxide, and many other poisons. They also can result from exposure to street drugs and from overdoses of antidepressants and other medications.

Seizures are often triggered by factors such as lack of sleep, alcohol consumption, stress, or hormonal changes associated with the menstrual cycle. These *seizure triggers* do not cause epilepsy but can provoke first seizures or cause breakthrough seizures in people who otherwise experience good seizure control with their medication. Sleep deprivation in particular is a universal and powerful trigger of seizures. For this reason, people with epilepsy should make sure to get enough sleep and should try to stay on a regular sleep schedule as much as possible. For some people, light flashing at a certain speed or the flicker of a computer monitor can trigger a seizure; this problem is called *photosensitive epilepsy*. Smoking cigarettes also can trigger seizures. The nicotine in cigarettes acts on receptors for the excitatory neurotransmitter acetylcholine in the brain, which increases neuronal firing. Seizures are not triggered by sexual activity except in very rare instances.

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What Are the Different Kinds of Seizures?

Doctors have described more than 30 different types of seizures. Seizures are divided into two major categories -- *focal seizures* and *generalized seizures*. However, there are many different types of seizures in each of these categories.

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Focal Seizures

Focal seizures, also called partial seizures, occur in just one part of the brain. About 60 percent of people with epilepsy have focal seizures. These seizures are frequently described by the area of the brain in which they originate. For example, someone might be diagnosed with focal frontal lobe seizures.

In a *simple focal seizure*, the person will remain conscious but experience unusual feelings or sensations that can take many forms. The person may experience sudden and unexplainable feelings of joy, anger, sadness, or nausea. He or she also may hear, smell, taste, see, or feel things that are not real.

In a *complex focal seizure*, the person has a change in or loss of consciousness. His or her consciousness may be altered, producing a dreamlike experience. People having a complex focal seizure may display strange, repetitious behaviors such as blinks, twitches, mouth movements, or even walking in a circle. These repetitious movements are called *automatisms*. More complicated actions, which may seem purposeful, can also occur involuntarily. Patients may also continue activities they started before the seizure began, such as washing dishes in a repetitive, unproductive fashion. These seizures usually last just a few seconds.

Some people with focal seizures, especially complex focal seizures, may experience *auras* -- unusual sensations that warn of an impending seizure. These auras are actually simple focal seizures in which the person maintains consciousness. The symptoms an individual person has, and the progression of those symptoms, tend to be *stereotyped*, or similar every time.

The symptoms of focal seizures can easily be confused with other disorders. For instance, the dreamlike perceptions associated with a complex focal seizure may be misdiagnosed as migraine headaches, which also may cause a dreamlike state. The strange behavior and sensations caused by focal seizures also can be mistaken for symptoms of narcolepsy, fainting, or even mental illness. It may take many tests and careful monitoring by an experienced physician to tell the difference between epilepsy and other disorders.

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Generalized Seizures

Generalized seizures are a result of abnormal neuronal activity on both sides of the brain. These seizures may cause loss of consciousness, falls, or massive muscle spasms.

There are many kinds of generalized seizures. In *absence seizures*, the person may appear to be staring into space and/or have jerking or twitching muscles. These seizures are sometimes referred to as *petit mal seizures*, which is an older term. *Tonic seizures* cause stiffening of muscles of the body, generally those in the

back, legs, and arms. *Clonic seizures* cause repeated jerking movements of muscles on both sides of the body. *Myoclonic seizures* cause jerks or twitches of the upper body, arms, or legs. *Atonic seizures* cause a loss of normal muscle tone. The affected person will fall down or may drop his or her head involuntarily. *Tonic-clonic seizures* cause a mixture of symptoms, including stiffening of the body and repeated jerks of the arms and/or legs as well as loss of consciousness. Tonic-clonic seizures are sometimes referred to by an older term: *grand mal seizures*.

Not all seizures can be easily defined as either focal or generalized. Some people have seizures that begin as focal seizures but then spread to the entire brain. Other people may have both types of seizures but with no clear pattern.

Society's lack of understanding about the many different types of seizures is one of the biggest problems for people with epilepsy. People who witness a non-convulsive seizure often find it difficult to understand that behavior which looks deliberate is not under the person's control. In some cases, this has led to the affected person being arrested or admitted to a psychiatric hospital. To combat these problems, people everywhere need to understand the many different types of seizures and how they may appear.

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What Are the Different Kinds of Epilepsy?

Just as there are many different kinds of seizures, there are many different kinds of epilepsy. Doctors have identified hundreds of different *epilepsy syndromes* -- disorders characterized by a specific set of symptoms that include epilepsy. Some of these syndromes appear to be hereditary. For other syndromes, the cause is unknown. Epilepsy syndromes are frequently described by their symptoms or by where in the brain they originate. People should discuss the implications of their type of epilepsy with their doctors to understand the full range of symptoms, the possible treatments, and the prognosis.

People with *absence epilepsy* have repeated absence seizures that cause momentary lapses of consciousness. These seizures almost always begin in childhood or adolescence, and they tend to run in families, suggesting that they may be at least partially due to a defective gene or genes. Some people with absence seizures have purposeless movements during their seizures, such as a jerking arm or rapidly blinking eyes. Others have no noticeable symptoms except for brief times when they are "out of it." Immediately after a seizure, the person can resume whatever he or she was doing. However, these seizures may occur so frequently that the person cannot concentrate in school or other situations. Childhood absence epilepsy usually stops when the child reaches puberty. Absence seizures usually have no lasting effect on intelligence or other brain functions.

Temporal lobe epilepsy, or TLE, is the most common epilepsy syndrome with focal seizures. These seizures are often associated with auras. TLE often begins in childhood. Research has shown that repeated temporal lobe seizures can cause a brain structure called the *hippocampus* to shrink over time. The hippocampus is important for memory and learning. While it may take years of temporal lobe seizures for measurable hippocampal damage to occur, this finding underlines the need to treat TLE early and as effectively as possible.

Neocortical epilepsy is characterized by seizures that originate from the brain's cortex, or outer layer. The seizures can be either focal or generalized. They may include strange sensations, visual hallucinations, emotional changes, muscle spasms, convulsions, and a variety of other symptoms, depending on where in the brain the seizures originate.

There are many other types of epilepsy, each with its own characteristic set of symptoms. Many of these, including *Lennox-Gastaut syndrome* and *Rasmussen's encephalitis*, begin in childhood. Children with Lennox-Gastaut syndrome have severe epilepsy with several different types of seizures, including atonic seizures, which cause sudden falls and are also called *drop attacks*. This severe form of epilepsy can be very difficult to treat effectively. Rasmussen's encephalitis is a progressive type of epilepsy in which half of the brain shows continual inflammation. It sometimes is treated with a radical surgical procedure called hemispherectomy ([see the section on Surgery](#)). Some childhood epilepsy syndromes, such as childhood absence epilepsy, tend to go into remission or stop entirely during adolescence, whereas other syndromes such as *juvenile myoclonic epilepsy* and *Lennox-Gastaut syndrome* are usually present for life once they develop. Seizure syndromes do not always appear in childhood, however.

Epilepsy syndromes that are easily treated, do not seem to impair cognitive functions or development, and usually stop spontaneously are often described as benign. Benign epilepsy syndromes include *benign infantile encephalopathy* and *benign neonatal convulsions*. Other syndromes, such as *early myoclonic encephalopathy*, include neurological and developmental problems. However, these problems may be caused by underlying neurodegenerative processes rather than by the seizures. Epilepsy syndromes in which the seizures and/or the person's cognitive abilities get worse over time are called *progressive epilepsy*.

Several types of epilepsy begin in infancy. The most common type of infantile epilepsy is *infantile spasms*, clusters of seizures that usually begin before the age of 6 months. During these seizures the infant may bend and cry out. Anticonvulsant drugs often do not work for infantile spasms, but the seizures can be treated with *ACTH* (adrenocorticotrophic hormone) or *prednisone*.

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When Are Seizures Not Epilepsy?

While any seizure is cause for concern, having a seizure does not by itself mean a person has epilepsy. First seizures, febrile seizures, nonepileptic events, and eclampsia are examples of seizures that may not be associated with epilepsy.

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First Seizures

Many people have a single seizure at some point in their lives. Often these seizures occur in reaction to anesthesia or a strong drug, but they also may be unprovoked, meaning that they occur without any obvious triggering factor. Unless the person has suffered brain damage or there is a family history of epilepsy or other neurological abnormalities, these single seizures usually are not followed by additional seizures. One recent study that followed patients for an average of 8 years found that only 33 percent of people have a second seizure within 4 years after an initial seizure. People who did not have a second seizure within that time remained seizure-free for the rest of the study. For people who did have a second seizure, the risk of a third seizure was about 73 percent on average by the end of 4 years.

When someone has experienced a first seizure, the doctor will usually order an *electroencephalogram*, or *EEG*, to determine what type of seizure the person may have had and if there are any detectable abnormalities in the person's brain waves. The doctor also may order brain scans to identify abnormalities that may be visible in the brain. These tests may help the doctor decide whether or not to treat the person with antiepileptic drugs. In some cases, drug treatment after the first seizure may help prevent future seizures and epilepsy. However, the drugs also can cause detrimental side effects, so doctors prescribe them only when they feel the benefits outweigh the risks. Evidence suggests that it may be beneficial to begin anticonvulsant medication once a person has had a second seizure, as the chance of future seizures increases significantly after this occurs.

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Febrile Seizures

Sometimes a child will have a seizure during the course of an illness with a high fever. These seizures are called *febrile seizures* (*febrile* is derived from the Latin word for "fever") and can be very alarming to the parents and other caregivers. In the past, doctors usually prescribed a course of anticonvulsant drugs following a febrile seizure in the hope of preventing epilepsy. However, most children who have a febrile seizure do not develop epilepsy, and long-term use of anticonvulsant drugs in children may damage the developing brain or cause other detrimental side effects. Experts at a 1980 consensus conference coordinated by the National Institutes of Health concluded that preventive treatment after a febrile seizure is generally not warranted unless certain other conditions are present: a family history of epilepsy, signs of nervous system impairment prior to the seizure, or a relatively prolonged or complicated seizure. The risk of subsequent non-febrile seizures is only 2 to 3 percent unless one of these factors is present.

Researchers have now identified several different genes that influence the risk of febrile seizures in certain families. Studying these genes may lead to new understanding of how febrile seizures occur and perhaps point to ways of preventing them.

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Nonepileptic Events

Sometimes people appear to have seizures, even though their brains show no seizure activity. This type of phenomenon has various names, including nonepileptic events and pseudoseizures. Both of these terms essentially mean something that looks like a seizure but isn't one. Nonepileptic events that are psychological in origin may be referred to as psychogenic seizures. Psychogenic seizures may indicate dependence, a need for attention, avoidance of stressful situations, or specific psychiatric conditions. Some people with epilepsy have psychogenic seizures in addition to their epileptic seizures. Other people who have psychogenic seizures do not have epilepsy at all. Psychogenic seizures cannot be treated in the same way as epileptic seizures. Instead, they are often treated by mental health specialists.

Other nonepileptic events may be caused by narcolepsy, Tourette syndrome, cardiac arrhythmia, and other medical conditions with symptoms that resemble seizures. Because symptoms of these disorders can look very much like epileptic seizures, they are often mistaken for epilepsy. Distinguishing between true epileptic seizures and nonepileptic events can be very difficult and requires a thorough medical assessment, careful monitoring, and knowledgeable health professionals. Improvements in brain scanning and monitoring technology may improve diagnosis of nonepileptic events in the future.

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Eclampsia

Eclampsia is a life-threatening condition that can develop in pregnant women. Its symptoms include sudden elevations of blood pressure and seizures. Pregnant women who develop unexpected seizures should be rushed to a hospital immediately. Eclampsia can be treated in a hospital setting and usually does not result in additional seizures or epilepsy once the pregnancy is over.

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How is Epilepsy Diagnosed?

Doctors have developed a number of different tests to determine whether a person has epilepsy and, if so, what kind of seizures the person has. In some cases, people may have symptoms that look very much like a seizure but in fact are nonepileptic events caused by other disorders. Even doctors may not be able to tell the difference between these disorders and epilepsy without close observation and intensive testing.

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EEG Monitoring

An EEG records brain waves detected by electrodes placed on the scalp. This is the most common diagnostic test for epilepsy and can detect abnormalities in the brain's electrical activity. People with epilepsy frequently have changes in their normal pattern of brain waves, even when they are not experiencing a seizure. While this type of test can be very useful in diagnosing epilepsy, it is not foolproof. Some people continue to show normal brain wave patterns even after they have experienced a seizure. In other cases, the unusual brain waves are generated deep in the brain where the EEG is unable to detect them. Many people who do not have epilepsy also show some unusual brain activity on an EEG. Whenever possible, an EEG should be performed within 24 hours of a patient's first seizure. Ideally, EEGs should be performed while the patient is sleeping as well as when he or she is awake, because brain activity during sleep is often quite different than at other times.

Video monitoring is often used in conjunction with EEG to determine the nature of a person's seizures. It also

can be used in some cases to rule out other disorders such as cardiac arrhythmia or narcolepsy that may look like epilepsy.

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Brain Scans

One of the most important ways of diagnosing epilepsy is through the use of brain scans. The most commonly used brain scans include *CT* (computed tomography), *PET* (positron emission tomography) and *MRI* (magnetic resonance imaging). *CT* and *MRI* scans reveal the structure of the brain, which can be useful for identifying brain tumors, cysts, and other structural abnormalities. *PET* and an adapted kind of *MRI* called *functional MRI* (*fMRI*) can be used to monitor the brain's activity and detect abnormalities in how it works. *SPECT* (*single photon emission computed tomography*) is a relatively new kind of brain scan that is sometimes used to locate seizure foci in the brain.

In some cases, doctors may use an experimental type of brain scan called a *magnetoencephalogram*, or *MEG*. *MEG* detects the magnetic signals generated by neurons to allow doctors to monitor brain activity at different points in the brain over time, revealing different brain functions. While *MEG* is similar in concept to *EEG*, it does not require electrodes and it can detect signals from deeper in the brain than an *EEG*. Doctors also are experimenting with brain scans called *magnetic resonance spectroscopy* (*MRS*) that can detect abnormalities in the brain's biochemical processes, and with *near-infrared spectroscopy*, a technique that can detect oxygen levels in brain tissue.

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Medical History

Taking a detailed medical history, including symptoms and duration of the seizures, is still one of the best methods available to determine if a person has epilepsy and what kind of seizures he or she has. The doctor will ask questions about the seizures and any past illnesses or other symptoms a person may have had. Since people who have suffered a seizure often do not remember what happened, caregivers' accounts of the seizure are vital to this evaluation.

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Blood Tests

Doctors often take blood samples for testing, particularly when they are examining a child. These blood samples are often screened for metabolic or genetic disorders that may be associated with the seizures. They also may be used to check for underlying problems such as infections, lead poisoning, anemia, and diabetes that may be causing or triggering the seizures.

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Developmental, Neurological, and Behavioral Tests

Doctors often use tests devised to measure motor abilities, behavior, and intellectual capacity as a way to determine how the epilepsy is affecting that person. These tests also can provide clues about what kind of epilepsy the person has.

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Can Epilepsy be Prevented?

Many cases of epilepsy can be prevented by wearing seatbelts and bicycle helmets, putting children in car seats, and other measures that prevent head injury and other trauma. Prescribing medication after first or second seizures or febrile seizures also may help prevent epilepsy in some cases. Good prenatal care,

including treatment of high blood pressure and infections during pregnancy, can prevent brain damage in the developing baby that may lead to epilepsy and other neurological problems later. Treating cardiovascular disease, high blood pressure, infections, and other disorders that can affect the brain during adulthood and aging also may prevent many cases of epilepsy. Finally, identifying the genes for many neurological disorders can provide opportunities for genetic screening and prenatal diagnosis that may ultimately prevent many cases of epilepsy.

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How can Epilepsy be Treated?

Accurate diagnosis of the type of epilepsy a person has is crucial for finding an effective treatment. There are many different ways to treat epilepsy. Currently available treatments can control seizures at least some of the time in about 80 percent of people with epilepsy. However, another 20 percent -- about 600,000 people with epilepsy in the United States -- have intractable seizures, and another 400,000 feel they get inadequate relief from available treatments. These statistics make it clear that improved treatments are desperately needed.

Doctors who treat epilepsy come from many different fields of medicine. They include neurologists, pediatricians, pediatric neurologists, internists, and family physicians, as well as neurosurgeons and doctors called epileptologists who specialize in treating epilepsy. People who need specialized or intensive care for epilepsy may be treated at large medical centers and neurology clinics at hospitals or by neurologists in private practice. Many epilepsy treatment centers are associated with university hospitals that perform research in addition to providing medical care.

Once epilepsy is diagnosed, it is important to begin treatment as soon as possible. Research suggests that medication and other treatments may be less successful in treating epilepsy once seizures and their consequences become established.

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Medications

By far the most common approach to treating epilepsy is to prescribe antiepileptic drugs. The first effective antiepileptic drugs were bromides, introduced by an English physician named Sir Charles Locock in 1857. He noticed that bromides had a sedative effect and seemed to reduce seizures in some patients. More than 20 different antiepileptic drugs are now on the market, all with different benefits and side effects. The choice of which drug to prescribe, and at what dosage, depends on many different factors, including the type of seizures a person has, the person's lifestyle and age, how frequently the seizures occur, and, for a woman, the likelihood that she will become pregnant. People with epilepsy should follow their doctor's advice and share any concerns they may have regarding their medication.

Doctors seeing a patient with newly developed epilepsy often prescribe carbamazepine, valproate, lamotrigine, oxcarbazepine, or phenytoin first, unless the epilepsy is a type that is known to require a different kind of treatment. For absence seizures, ethosuximide is often the primary treatment. Other commonly prescribed drugs include clonazepam, phenobarbital, and primidone. Some relatively new epilepsy drugs include tiagabine, gabapentin, topiramate, levetiracetam, and felbamate. Other drugs are used in combination with one of the standard drugs or for intractable seizures that do not respond to other medications. A few drugs, such as fosphenytoin, are approved for use only in hospital settings to treat specific problems such as *status epilepticus* (see section, "Are There Special Risks Associated With Epilepsy?"). For people with stereotyped recurrent severe seizures that can be easily recognized by the person's family, the drug diazepam is now available as a gel that can be administered rectally by a family member. This method of drug delivery may be able to stop prolonged or repeated seizures before they develop into *status epilepticus*.

For most people with epilepsy, seizures can be controlled with just one drug at the optimal dosage. Combining medications usually amplifies side effects such as fatigue and decreased appetite, so doctors usually prescribe *monotherapy*, or the use of just one drug, whenever possible. Combinations of drugs are sometimes prescribed if monotherapy fails to effectively control a patient's seizures.

The number of times a person needs to take medication each day is usually determined by the drug's half-life, or the time it takes for half the drug dose to be *metabolized* or broken down into other substances in the body. Some drugs, such as phenytoin and phenobarbital, only need to be taken once a day, while others such as valproate must be taken two or three times a day.

Most side effects of antiepileptic drugs are relatively minor, such as fatigue, dizziness, or weight gain. However, severe and life-threatening side effects such as allergic reactions can occur. Epilepsy medication also may predispose people to developing depression or psychoses. People with epilepsy should consult a doctor immediately if they develop any kind of rash while on medication, or if they find themselves depressed or otherwise unable to think in a rational manner. Other danger signs that should be discussed with a doctor immediately are extreme fatigue, staggering or other movement problems, and slurring of words. People with epilepsy should be aware that their epilepsy medication can interact with many other drugs in potentially harmful ways. For this reason, people with epilepsy should always tell doctors who treat them which medications they are taking. Women also should know that some antiepileptic drugs can interfere with the effectiveness of oral contraceptives, and they should discuss this possibility with their doctors.

Since people can become more sensitive to medications as they age, they may need to have their blood levels of medication checked occasionally to see if the dose needs to be adjusted. The effects of a particular medication also sometimes wear off over time, leading to an increase in seizures if the dose is not adjusted. People should know that some citrus fruit, in particular grapefruit juice, may interfere with breakdown of many drugs. This can cause too much of the drug to build up in their bodies, often worsening the side effects.

People taking epilepsy medication should be sure to check with their doctor and/or seek a second medical opinion if their medication does not appear to be working or if it causes unexpected side effects.

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Tailoring the dosage of antiepileptic drugs

When a person starts a new epilepsy drug, it is important to tailor the dosage to achieve the best results. People's bodies react to medications in very different and sometimes unpredictable ways, so it may take some time to find the right drug at the right dose to provide optimal control of seizures while minimizing side effects. A drug that has no effect or very bad side effects at one dose may work very well at another dose. Doctors will usually prescribe a low dose of the new drug initially and monitor blood levels of the drug to determine when the best possible dose has been reached.

Generic versions are available for many antiepileptic drugs. The chemicals in generic drugs are exactly the same as in the brand-name drugs, but they may be absorbed or processed differently in the body because of the way they are prepared. Therefore, patients should always check with their doctors before switching to a generic version of their medication.

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Discontinuing medication

Some doctors will advise people with epilepsy to discontinue their antiepileptic drugs after 2 years have passed without a seizure. Others feel it is better to wait for 4 to 5 years. Discontinuing medication should **always** be done with a doctor's advice and supervision. It is very important to continue taking epilepsy medication for as long as the doctor prescribes it. People also should ask the doctor or pharmacist ahead of time what they should do if they miss a dose. Discontinuing medication without a doctor's advice is one of the major reasons people who have been seizure-free begin having new seizures. Seizures that result from suddenly stopping medication can be very serious and can lead to status epilepticus. Furthermore, there is some evidence that uncontrolled seizures trigger changes in neurons that can make it more difficult to treat the seizures in the future.

The chance that a person will eventually be able to discontinue medication varies depending on the person's age and his or her type of epilepsy. More than half of children who go into remission with medication can

eventually stop their medication without having new seizures. One study showed that 68 percent of adults who had been seizure-free for 2 years before stopping medication were able to do so without having more seizures and 75 percent could successfully discontinue medication if they had been seizure-free for 3 years. However, the odds of successfully stopping medication are not as good for people with a family history of epilepsy, those who need multiple medications, those with focal seizures, and those who continue to have abnormal EEG results while on medication.

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Surgery

When seizures cannot be adequately controlled by medications, doctors may recommend that the person be evaluated for surgery. Surgery for epilepsy is performed by teams of doctors at medical centers. To decide if a person may benefit from surgery, doctors consider the type or types of seizures he or she has. They also take into account the brain region involved and how important that region is for everyday behavior. Surgeons usually avoid operating in areas of the brain that are necessary for speech, language, hearing, or other important abilities. Doctors may perform tests such as a Wada test (administration of the drug amobarbital into the carotid artery) to find areas of the brain that control speech and memory. They often monitor the patient intensively prior to surgery in order to pinpoint the exact location in the brain where seizures begin. They also may use implanted electrodes to record brain activity from the surface of the brain. This yields better information than an external EEG.

A 1990 National Institutes of Health consensus conference on surgery for epilepsy concluded that there are three broad categories of epilepsy that can be treated successfully with surgery. These include focal seizures, seizures that begin as focal seizures before spreading to the rest of the brain, and unilateral multifocal epilepsy with infantile hemiplegia (such as Rasmussen's encephalitis). Doctors generally recommend surgery only after patients have tried two or three different medications without success, or if there is an identifiable brain *lesion*--a damaged or dysfunctional area--believed to cause the seizures.

A study published in 2000 compared surgery to an additional year of treatment with antiepileptic drugs in people with longstanding temporal lobe epilepsy. The results showed that 64 percent of patients receiving surgery became seizure-free, compared to 8 percent of those who continued with medication only. Because of this study and other evidence, the American Academy of Neurology (AAN) now recommends surgery for TLE when antiepileptic drugs are not effective. However, the study and the AAN guidelines do not provide guidance on how long seizures should occur, how severe they should be, or how many drugs should be tried before surgery is considered. A nationwide study is now underway to determine how soon surgery for TLE should be performed.

If a person is considered a good candidate for surgery and has seizures that cannot be controlled with available medication, experts generally agree that surgery should be performed as early as possible. It can be difficult for a person who has had years of seizures to fully re-adapt to a seizure-free life if the surgery is successful. The person may never have had an opportunity to develop independence, and he or she may have had difficulties with school and work that could have been avoided with earlier treatment. Surgery should always be performed with support from rehabilitation specialists and counselors who can help the person deal with the many psychological, social, and employment issues he or she may face.

While surgery can significantly reduce or even halt seizures for some people, it is important to remember that any kind of surgery carries some amount of risk (usually small). Surgery for epilepsy does not always successfully reduce seizures and it can result in cognitive or personality changes, even in people who are excellent candidates for surgery. Patients should ask their surgeon about his or her experience, success rates, and complication rates with the procedure they are considering.

Even when surgery completely ends a person's seizures, it is important to continue taking seizure medication for some time to give the brain time to re-adapt. Doctors generally recommend medication for 2 years after a successful operation to avoid new seizures.

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Surgery to treat underlying conditions

In cases where seizures are caused by a brain tumor, hydrocephalus, or other conditions that can be treated with surgery, doctors may operate to treat these underlying conditions. In many cases, once the underlying condition is successfully treated, a person's seizures will disappear as well.

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Surgery to remove a seizure focus

The most common type of surgery for epilepsy is removal of a *seizure focus*, or small area of the brain where seizures originate. This type of surgery, which doctors may refer to as a *lobectomy* or *lesionectomy*, is appropriate only for focal seizures that originate in just one area of the brain. In general, people have a better chance of becoming seizure-free after surgery if they have a small, well-defined seizure focus. Lobectomies have a 55-70 percent success rate when the type of epilepsy and the seizure focus is well-defined. The most common type of lobectomy is a *temporal lobe resection*, which is performed for people with temporal lobe epilepsy. Temporal lobe resection leads to a significant reduction or complete cessation of seizures about 70 - 90 percent of the time.

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Multiple subpial transection

When seizures originate in part of the brain that cannot be removed, surgeons may perform a procedure called a *multiple subpial transection*. In this type of operation, which has been commonly performed since 1989, surgeons make a series of cuts that are designed to prevent seizures from spreading into other parts of the brain while leaving the person's normal abilities intact. About 70 percent of patients who undergo a multiple subpial transection have satisfactory improvement in seizure control.

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Corpus callosotomy

Corpus callosotomy, or severing the network of neural connections between the right and left halves, or *hemispheres*, of the brain, is done primarily in children with severe seizures that start in one half of the brain and spread to the other side. Corpus callosotomy can end drop attacks and other generalized seizures. However, the procedure does not stop seizures in the side of the brain where they originate, and these focal seizures may even increase after surgery.

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Hemispherectomy and hemispherotomy

These procedures remove half of the brain's cortex, or outer layer. They are used predominantly in children who have seizures that do not respond to medication because of damage that involves only half the brain, as occurs with conditions such as Rasmussen's encephalitis, Sturge-Weber syndrome, and hemimegencephaly. While this type of surgery is very radical and is performed only as a last resort, children often recover very well from the procedure, and their seizures usually cease altogether. With intense rehabilitation, they often recover nearly normal abilities. Since the chance of a full recovery is best in young children, hemispherectomy should be performed as early in a child's life as possible. It is rarely performed in children older than 13.

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Devices

The vagus nerve stimulator was approved by the U.S. Food and Drug Administration (FDA) in 1997 for use in

people with seizures that are not well-controlled by medication. The vagus nerve stimulator is a battery-powered device that is surgically implanted under the skin of the chest, much like a pacemaker, and is attached to the vagus nerve in the lower neck. This device delivers short bursts of electrical energy to the brain via the vagus nerve. On average, this stimulation reduces seizures by about 20 - 40 percent. Patients usually cannot stop taking epilepsy medication because of the stimulator, but they often experience fewer seizures and they may be able to reduce the dose of their medication. Side effects of the vagus nerve stimulator are generally mild but may include hoarseness, ear pain, a sore throat, or nausea. Adjusting the amount of stimulation can usually eliminate most side effects, although the hoarseness typically persists. The batteries in the vagus nerve stimulator need to be replaced about once every 5 years; this requires a minor operation that can usually be performed as an outpatient procedure.

Several new devices may become available for epilepsy in the future. Researchers are studying whether *transcranial magnetic stimulation (TMS)*, a procedure which uses a strong magnet held outside the head to influence brain activity, may reduce seizures. They also hope to develop implantable devices that can deliver drugs to specific parts of the brain.

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Diet

Studies have shown that, in some cases, children may experience fewer seizures if they maintain a strict diet rich in fats and low in carbohydrates. This unusual diet, called the *ketogenic diet*, causes the body to break down fats instead of carbohydrates to survive. This condition is called ketosis. One study of 150 children whose seizures were poorly controlled by medication found that about one-fourth of the children had a 90 percent or better decrease in seizures with the ketogenic diet, and another half of the group had a 50 percent or better decrease in their seizures. Moreover, some children can discontinue the ketogenic diet after several years and remain seizure-free. The ketogenic diet is not easy to maintain, as it requires strict adherence to an unusual and limited range of foods. Possible side effects include retarded growth due to nutritional deficiency and a buildup of uric acid in the blood, which can lead to kidney stones. People who try the ketogenic diet should seek the guidance of a dietician to ensure that it does not lead to serious nutritional deficiency.

Researchers are not sure how ketosis inhibits seizures. One study showed that a byproduct of ketosis called beta-hydroxybutyrate (BHB) inhibits seizures in animals. If BHB also works in humans, researchers may eventually be able to develop drugs that mimic the seizure-inhibiting effects of the ketogenic diet.

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Other Treatment Strategies

Researchers are studying whether biofeedback -- a strategy in which individuals learn to control their own brain waves -- may be useful in controlling seizures. However, this type of therapy is controversial and most studies have shown discouraging results. Taking large doses of vitamins generally does not help a person's seizures and may even be harmful in some cases. But a good diet and some vitamin supplements, particularly folic acid, may help reduce some birth defects and medication-related nutritional deficiencies. Use of non-vitamin supplements such as melatonin is controversial and can be risky. One study showed that melatonin may reduce seizures in some children, while another found that the risk of seizures increased measurably with melatonin. Most non-vitamin supplements such as those found in health food stores are not regulated by the FDA, so their true effects and their interactions with other drugs are largely unknown.

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How Does Epilepsy Affect Daily Life?

Most people with epilepsy lead outwardly normal lives. Approximately 80 percent can be significantly helped by modern therapies, and some may go months or years between seizures. However, the condition can and does affect daily life for people with epilepsy, their family, and their friends. People with severe seizures that resist treatment have, on average, a shorter life expectancy and an increased risk of cognitive impairment, particularly

if the seizures developed in early childhood. These impairments may be related to the underlying conditions that cause epilepsy or to epilepsy treatment rather than the epilepsy itself.

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Behavior and Emotions

It is not uncommon for people with epilepsy, especially children, to develop behavioral and emotional problems. Sometimes these problems are caused by embarrassment or frustration associated with epilepsy. Other problems may result from bullying, teasing, or avoidance in school and other social settings. In children, these problems can be minimized if parents encourage a positive outlook and independence, do not reward negative behavior with unusual amounts of attention, and try to stay attuned to their child's needs and feelings. Families must learn to accept and live with the seizures without blaming or resenting the affected person. Counseling services can help families cope with epilepsy in a positive manner. Epilepsy support groups also can help by providing a way for people with epilepsy and their family members to share their experiences, frustrations, and tips for coping with the disorder.

People with epilepsy have an increased risk of poor self-esteem, depression, and suicide. These problems may be a reaction to a lack of understanding or discomfort about epilepsy that may result in cruelty or avoidance by other people. Many people with epilepsy also live with an ever-present fear that they will have another seizure.

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Driving and Recreation

For many people with epilepsy, the risk of seizures restricts their independence, in particular the ability to drive. Most states and the District of Columbia will not issue a driver's license to someone with epilepsy unless the person can document that they have gone a specific amount of time without a seizure (the waiting period varies from a few months to several years). Some states make exceptions for this policy when seizures don't impair consciousness, occur only during sleep, or have long auras or other warning signs that allow the person to avoid driving when a seizure is likely to occur. Studies show that the risk of having a seizure-related accident decreases as the length of time since the last seizure increases. One study found that the risk of having a seizure-related motor vehicle accident is 93 percent less in people who wait at least 1 year after their last seizure before driving, compared to people who wait for shorter intervals.

The risk of seizures also restricts people's recreational choices. For instance, people with epilepsy should not participate in sports such as skydiving or motor racing where a moment's inattention could lead to injury. Other activities, such as swimming and sailing, should be done only with precautions and/or supervision. However, jogging, football, and many other sports are reasonably safe for a person with epilepsy. Studies to date have not shown any increase in seizures due to sports, although these studies have not focused on any activity in particular. There is some evidence that regular exercise may even improve seizure control in some people. Sports are often such a positive factor in life that it is best for the person to participate, although the person with epilepsy and the coach or other leader should take appropriate safety precautions. It is important to take steps to avoid potential sports-related problems such as dehydration, overexertion, and hypoglycemia, as these problems can increase the risk of seizures.

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Education and Employment

By law, people with epilepsy or other handicaps in the United States cannot be denied employment or access to any educational, recreational, or other activity because of their seizures. However, one survey showed that only about 56 percent of people with epilepsy finish high school and about 15 percent finish college -- rates much lower than those for the general population. The same survey found that about 25 percent of working-age people with epilepsy are unemployed. These numbers indicate that significant barriers still exist for people with epilepsy in school and work. Restrictions on driving limit the employment opportunities for many people.

with epilepsy, and many find it difficult to face the misunderstandings and social pressures they encounter in public situations. Antiepileptic drugs also may cause side effects that interfere with concentration and memory. Children with epilepsy may need extra time to complete schoolwork, and they sometimes may need to have instructions or other information repeated for them. Teachers should be told what to do if a child in their classroom has a seizure, and parents should work with the school system to find reasonable ways to accommodate any special needs their child may have.

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Pregnancy and Motherhood

Women with epilepsy are often concerned about whether they can become pregnant and have a healthy child. This is usually possible. While some seizure medications and some types of epilepsy may reduce a person's interest in sexual activity, most people with epilepsy can become pregnant. Moreover, women with epilepsy have a 90 percent or better chance of having a normal, healthy baby, and the risk of birth defects is only about 4 to 6 percent. The risk that children of parents with epilepsy will develop epilepsy themselves is only about 5 percent unless the parent has a clearly hereditary form of the disorder. Parents who are worried that their epilepsy may be hereditary may wish to consult a genetic counselor to determine what the risk might be. Amniocentesis and high-level ultrasound can be performed during pregnancy to ensure that the baby is developing normally, and a procedure called a maternal serum alpha-fetoprotein test can be used for prenatal diagnosis of many conditions if a problem is suspected.

There are several precautions women can take before and during pregnancy to reduce the risks associated with pregnancy and delivery. Women who are thinking about becoming pregnant should talk with their doctors to learn any special risks associated with their epilepsy and the medications they may be taking. Some seizure medications, particularly valproate, trimethidone, and phenytoin, are known to increase the risk of having a child with birth defects such as cleft palate, heart problems, or finger and toe defects. For this reason, a woman's doctor may advise switching to other medications during pregnancy. Whenever possible, a woman should allow her doctor enough time to properly change medications, including phasing in the new medications and checking to determine when blood levels are stabilized, before she tries to become pregnant. Women should also begin prenatal vitamin supplements -- especially with folic acid, which may reduce the risk of some birth defects -- well before pregnancy. Women who discover that they are pregnant but have not already spoken with their doctor about ways to reduce the risks should do so as soon as possible. However, they should continue taking seizure medication as prescribed until that time to avoid preventable seizures. Seizures during pregnancy can harm the developing baby or lead to miscarriage, particularly if the seizures are severe. Nevertheless, many women who have seizures during pregnancy have normal, healthy babies.

Women with epilepsy sometimes experience a change in their seizure frequency during pregnancy, even if they do not change medications. About 25 to 40 percent of women have an increase in their seizure frequency while they are pregnant, while other women may have fewer seizures during pregnancy. The frequency of seizures during pregnancy may be influenced by a variety of factors, including the woman's increased blood volume during pregnancy, which can dilute the effect of medication. Women should have their blood levels of seizure medications monitored closely during and after pregnancy, and the medication dosage should be adjusted accordingly.

Pregnant women with epilepsy should take prenatal vitamins and get plenty of sleep to avoid seizures caused by sleep deprivation. They also should take vitamin K supplements after 34 weeks of pregnancy to reduce the risk of a blood-clotting disorder in infants called neonatal coagulopathy that can result from fetal exposure to epilepsy medications. Finally, they should get good prenatal care, avoid tobacco, caffeine, alcohol, and illegal drugs, and try to avoid stress.

Labor and delivery usually proceed normally for women with epilepsy, although there is a slightly increased risk of hemorrhage, eclampsia, premature labor, and cesarean section. Doctors can administer antiepileptic drugs intravenously and monitor blood levels of anticonvulsant medication during labor to reduce the risk that the labor will trigger a seizure. Babies sometimes have symptoms of withdrawal from the mother's seizure medication after they are born, but these problems wear off in a few weeks or months and usually do not cause serious or long-term effects. A mother's blood levels of anticonvulsant medication should be checked

frequently after delivery as medication often needs to be decreased.

Epilepsy medications need not influence a woman's decision about breast-feeding her baby. Only minor amounts of epilepsy medications are secreted in breast milk, usually not enough to harm the baby and much less than the baby was exposed to in the womb. On rare occasions, the baby may become excessively drowsy or feed poorly, and these problems should be closely monitored. However, experts believe the benefits of breast-feeding outweigh the risks except in rare circumstances.

To increase doctors' understanding of how different epilepsy medications affect pregnancy and the chances of having a healthy baby, Massachusetts General Hospital has begun a nationwide registry for women who take antiepileptic drugs while pregnant. Women who enroll in this program are given educational materials on pre-conception planning and perinatal care and are asked to provide information about the health of their children (this information is kept confidential). Women and physicians can contact this registry by calling 1-888-233-2334 or 617-726-1742 (fax: 617-724-8307).

Women with epilepsy should be aware that some epilepsy medications can interfere with the effectiveness of oral contraceptives. Women who wish to use oral contraceptives to prevent pregnancy should discuss this with their doctors, who may be able to prescribe a different kind of antiepileptic medication or suggest other ways of avoiding an unplanned pregnancy.

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Are There Special Risks Associated With Epilepsy?

Although most people with epilepsy lead full, active lives, they are at special risk for two life-threatening conditions: status epilepticus and sudden unexplained death.

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Status Epilepticus

Status epilepticus is a potentially life-threatening condition in which a person either has an abnormally prolonged seizure or does not fully regain consciousness between seizures. Although there is no strict definition for the time at which a seizure turns into status epilepticus, most people agree that any seizure lasting longer than 5 minutes should, for practical purposes, be treated as though it was status epilepticus.

Status epilepticus affects about 195,000 people each year in the United States and results in about 42,000 deaths. While people with epilepsy are at an increased risk for status epilepticus, about 60 percent of people who develop this condition have no previous seizure history. These cases often result from tumors, trauma, or other problems that affect the brain and may themselves be life-threatening.

While most seizures do not require emergency medical treatment, someone with a prolonged seizure lasting more than 5 minutes may be in status epilepticus and should be taken to an emergency room immediately. It is important to treat a person with status epilepticus as soon as possible. One study showed that 80 percent of people in status epilepticus who received medication within 30 minutes of seizure onset eventually stopped having seizures, whereas only 40 percent recovered if 2 hours had passed before they received medication. Doctors in a hospital setting can treat status epilepticus with several different drugs and can undertake emergency life-saving measures, such as administering oxygen, if necessary.

People in status epilepticus do not always have severe convulsive seizures. Instead, they may have repeated or prolonged nonconvulsive seizures. This type of status epilepticus may appear as a sustained episode of confusion or agitation in someone who does not ordinarily have that kind of mental impairment. While this type of episode may not seem as severe as convulsive status epilepticus, it should still be treated as an emergency.

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Sudden Unexplained Death

For reasons that are poorly understood, people with epilepsy have an increased risk of dying suddenly for no discernible reason. This condition, called *sudden unexplained death*, can occur in people without epilepsy, but epilepsy increases the risk about two-fold. Researchers are still unsure why sudden unexplained death occurs. One study suggested that use of more than two anticonvulsant drugs may be a risk factor. However, it is not clear whether the use of multiple drugs causes the sudden death, or whether people who use multiple anticonvulsants have a greater risk of death because they have more severe types of epilepsy.

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What Research Is Being Done on Epilepsy?

While research has led to many advances in understanding and treating epilepsy, there are many unanswered questions about how and why seizures develop, how they can best be treated or prevented, and how they influence other brain activity and brain development. Researchers, many of whom are supported by the National Institute of Neurological Disorders and Stroke (NINDS), are studying all of these questions. They also are working to identify and test new drugs and other treatments for epilepsy and to learn how those treatments affect brain activity and development.

The NINDS's Anticonvulsant Screening Program (ASP) studies potential new therapies with the goal of enhancing treatment for patients with epilepsy. Since it began in 1975, more than 390 public-private partnerships have been created. These partnerships have resulted in state-of-the-art evaluations of more than 25,000 compounds for their potential as antiepileptic drugs. This government-sponsored effort has contributed to the development of five drugs that are now approved for use in the United States. It has also aided in the discovery and profiling of six new compounds currently in various stages of clinical development. Besides testing for safer, more efficacious therapies, the Program is developing and validating new models that may one day find therapies that intervene in the disease process itself as well as models of resistant or refractory epilepsy.

Scientists continue to study how excitatory and inhibitory neurotransmitters interact with brain cells to control nerve firing. They can apply different chemicals to cultures of neurons in laboratory dishes to study how those chemicals influence neuronal activity. They also are studying how glia and other non-neuronal cells in the brain contribute to seizures. This research may lead to new drugs and other new ways of treating seizures.

Researchers also are working to identify genes that may influence epilepsy in some way. Identifying these genes can reveal the underlying chemical processes that influence epilepsy and point to new ways of preventing or treating this disorder. Researchers also can study rats and mice that have missing or abnormal copies of certain genes to determine how these genes affect normal brain development and resistance to damage from disease and other environmental factors. In the future, researchers may be able to use panels of gene fragments, called "gene chips," to determine each person's genetic makeup. This information may allow doctors to prevent epilepsy or to predict which treatments will be most beneficial.

Doctors are now experimenting with several new types of therapies for epilepsy. In one preliminary clinical trial, doctors have begun transplanting fetal pig neurons that produce GABA into the brains of patients to learn whether the cell transplants can help control seizures. Preliminary research suggests that stem cell transplants also may prove beneficial for treating epilepsy. Research showing that the brain undergoes subtle changes prior to a seizure has led to a prototype device that may be able to predict seizures up to 3 minutes before they begin. If this device works, it could greatly reduce the risk of injury from seizures by allowing people to move to a safe area before their seizures start. This type of device also may be hooked up to a treatment pump or other device that will automatically deliver an antiepileptic drug or an electric impulse to forestall the seizures.

Researchers are continually improving MRI and other brain scans. Pre-surgical brain imaging can guide doctors to abnormal brain tissue and away from essential parts of the brain. Researchers also are using brain scans such as magnetoencephalograms (MEG) and magnetic resonance spectroscopy (MRS) to identify and study subtle problems in the brain that cannot otherwise be detected. Their findings may lead to a better understanding of epilepsy and how it can be treated.

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How Can I Help Research on Epilepsy?

There are many ways that people with epilepsy and their families can help with research on this disorder. Pregnant women with epilepsy who are taking antiepileptic drugs can help researchers learn how these drugs affect unborn children by participating in the Antiepileptic Drug Pregnancy Registry, which is maintained by the Genetics and Teratology Unit of Massachusetts General Hospital ([see section on Pregnancy and Motherhood](#)). People with epilepsy that may be hereditary can aid research by participating in the Epilepsy Gene Discovery Project, which is supported by the Epilepsy Foundation. This project helps to educate people with epilepsy about new genetic research on the disorder and enlists families with hereditary epilepsy for participation in gene research. People who enroll in this project are asked to create a family tree showing which people in their family have or have had epilepsy. Researchers then examine this information to determine if the epilepsy is in fact hereditary, and they may invite participants to enroll in genetic research studies. In many cases, identifying the gene defect responsible for epilepsy in an individual family leads researchers to new clues about how epilepsy develops. It also can provide opportunities for early diagnosis and genetic screening of individuals in the family.

People with epilepsy can help researchers test new medications, surgical techniques, and other treatments by enrolling in clinical trials. Information on clinical trials can be obtained from the NINDS as well as many private pharmaceutical and biotech companies, universities, and other organizations. A person who wishes to participate in a clinical trial must ask his or her regular physician to refer him or her to the doctor in charge of that trial and to forward all necessary medical records. While experimental therapies may benefit those who participate in clinical trials, patients and their families should remember that all clinical trials also involve some risks. Therapies being tested in clinical trials may not work, and in some cases doctors may not yet be sure that the therapies are safe. Patients should be certain they understand the risks before agreeing to participate in a clinical trial.

Patients and their families also can help epilepsy research by donating their brain to a brain bank after death. Brain banks supply researchers with tissue they can use to study epilepsy and other disorders. Below are some brain banks that accept tissue from patients with epilepsy:

Brain and Tissue Bank for Developmental Disorders

University of Maryland
655 West Baltimore Street, Room 10-035 BRB
Baltimore, MD 21201-1559
800-847-1539
E-mail: btbumab@umaryland.edu
<http://medschool.umaryland.edu/BTBank/>

(tissue from children only)

Brain and Tissue Bank for Developmental Disorders

University of Miami
Department of Pathology, R-5
Papanicolaou Building, Room 410
Miami, FL 33136
800-59BRAIN (592-7246)
E-mail: btb@med.miami.edu
www.miami.edu/braintissue-bank

(tissue from adults only)

Brain Endowment Bank

University of Miami
1501 NW Ninth Avenue, Suite #4013
Miami, FL 33136
305-243-6219
800-UM-BRAIN (862-7246)

National Disease Research Interchange

8 Penn Center, 8th Floor
Philadelphia, PA 19103
215-557-7361
800-222-NDRI (6374)
E-mail: htor@ndri.com
www.ndri.com

Human Brain and Spinal Fluid Resource Center

Neurology Research (127A)
W. Los Angeles Healthcare Center
11301 Wilshire Boulevard
Los Angeles, CA 90073
310-268-3536
Page: 310-636-5199
E-mail: RMNbbank@ucla.edu
www.loni.ucla.edu/~nnrsb/NNRSB

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What To Do If You See Someone Having a Seizure

If you see someone having a seizure with convulsions and/or loss of consciousness, here's how you can help:

1. Roll the person on his or her side to prevent choking on any fluids or vomit.
2. Cushion the person's head.
3. Loosen any tight clothing around the neck.
4. Keep the person's airway open. If necessary, grip the person's jaw gently and tilt his or her head back.
5. Do NOT restrict the person from moving unless he or she is in danger.
6. Do NOT put anything into the person's mouth, not even medicine or liquid. These can cause choking or damage to the person's jaw, tongue, or teeth. Contrary to widespread belief, people cannot swallow their tongues during a seizure or any other time.
7. Remove any sharp or solid objects that the person might hit during the seizure.
8. Note how long the seizure lasts and what symptoms occurred so you can tell a doctor or emergency personnel if necessary.
9. Stay with the person until the seizure ends.

Call 911 if:

The person is pregnant or has diabetes.

The seizure happened in water.

The seizure lasts longer than 5 minutes.

The person does not begin breathing again or does not return to consciousness after the seizure stops.

Another seizure starts before the person regains consciousness.

The person injures himself or herself during the seizure.

This is a first seizure or you think it might be. If in doubt, check to see if the person has a medical identification card or jewelry stating that they have epilepsy or a seizure disorder.

After the seizure ends, the person will probably be groggy and tired. He or she also may have a headache and be confused or embarrassed. Be patient with the person and try to help him or her find a place to rest if he or she is tired or doesn't feel well. If necessary, offer to call a taxi, a friend, or a relative to help the person get home safely.

If you see someone having a non-convulsive seizure, remember that the person's behavior is not intentional. The person may wander aimlessly or make alarming or unusual gestures. You can help by following these guidelines:

Remove any dangerous objects from the area around the person or in his or her path.

Don't try to stop the person from wandering unless he or she is in danger.

Don't shake the person or shout.

Stay with the person until he or she is completely alert.

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Conclusion

Many people with epilepsy lead productive and outwardly normal lives. Medical and research advances in the past two decades have led to a better understanding of epilepsy and seizures than ever before. Advanced brain scans and other techniques allow greater accuracy in diagnosing epilepsy and determining when a patient may be helped by surgery. More than 20 different medications and a variety of surgical techniques are now available and provide good control of seizures for most people with epilepsy. Other treatment options include the ketogenic diet and the first implantable device, the vagus nerve stimulator. Research on the underlying causes of epilepsy, including identification of genes for some forms of epilepsy and febrile seizures, has led to a greatly improved understanding of epilepsy that may lead to more effective treatments or even new ways of preventing epilepsy in the future.

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Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
(800) 352-9424
<http://www.ninds.nih.gov>

Information also is available from the following organizations:

Citizens United for Research in Epilepsy (CURE)
730 North Franklin Street
Suite 404
Chicago, IL 60654
info@CUREepilepsy.org
<http://www.CUREepilepsy.org>
Tel: 312-255-1801
Fax: 312-255-1809
Non-profit grassroots organization formed by parents and families to raise funds for epilepsy research.

Epilepsy Foundation
8301 Professional Place
Landover, MD 20785-7223
postmaster@efa.org
<http://www.epilepsyfoundation.org>
Tel: 301-459-3700 800-EFA-1000 (332-1000)
Fax: 301-577-2684
National charitable organization dedicated to the welfare of people with epilepsy. Works for children and adults affected by seizures through education, advocacy, services, and research towards a cure. Offers a Legal Defense Program through a fund.

Epilepsy Institute
257 Park Avenue South
New York, NY 10010

People Against Childhood Epilepsy (PACE)
7 East 85th Street
Suite A3

website@epilepsvinstitute.org
<http://www.epilepsvinstitute.org>

Tel: 212-677-8550
Fax: 212-677-5825
Non-profit organization that provides comprehensive social services and resources for people with epilepsy and their families.

New York, NY 10028
pacenvemail@aol.com
<http://www.paceusa.org>

Tel: 212-665-PACE (7223)
Fax: 212-327-3075
Non-profit research resource that provides information and support to families of children with epilepsy.

Family Caregiver Alliance/ National Center on Caregiving

180 Montgomery Street
Suite 1100
San Francisco, CA 94104
info@caregiver.org
<http://www.caregiver.org>

Tel: 415-434-3388 800-445-8106
Fax: 415-434-3508
Supports and assists families and caregivers of adults with debilitating health conditions. Offers programs and consultation on caregiving issues at local, state, and national levels. Offers free publications and support online, including a national directory of publicly funded caregiver support programs.

National Council on Patient Information and Education

200-A Monroe Street
Suite 201
Rockville, MD 20850
ncpie@ncpie.info
<http://www.talkaboutrx.org>

Tel: 301-340-3940
Fax: 301-340-3944
Coalition of nearly 150 organizations committed to safer, more effective medicine use through better communication. Additional website is www.bemedwise.org.

National Family Caregivers Association

10400 Connecticut Avenue
Suite 500
Kensington, MD 20895-3944
info@thefamilycaregiver.org
<http://www.thefamilycaregiver.org>

Tel: 800-896-3650
Fax: 301-942-2302
Grassroots organization dedicated to supporting and improving the lives of America's family caregivers. Created to educate, support, empower, and advocate for the millions of Americans who care for their ill, aged, or disabled loved ones.

National Organization for Rare Disorders (NORD)

P.O. Box 1968
(55 Kenosia Avenue)
Danbury, CT 06813-1968
orphan@rarediseases.org
<http://www.rarediseases.org>

Tel: 203-744-0100 Voice Mail 800-999-NORD (6673)
Fax: 203-798-2291
Federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. Committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service.

International RadioSurgery Association

3002 N. Second Street
Harrisburg, PA 17110
office1@irsa.org
<http://www.irsa.org>

Tel: 717-260-9808
Fax: 717-260-9809
Proactive patient organization providing information and referrals on Gamma Knife, Linac, and particle beam radiosurgery for brain tumors, arteriovenous malformations (AVMs), and neurological pain and movement disorders.

Charlie Foundation to Help Cure Pediatric Epilepsy

1223 Wilshire Blvd.
Suite #815
Santa Monica, CA 90403
ketoman@aol.com
<http://www.charliefoundation.org>

Tel: 310-393-2347
Fax: 310-453-4585
Non-profit organization that raises money for scientific research focusing on the ketogenic diet. Offers education programs and materials for families and dieticians.

Epilepsy Therapy Project

P.O. Box 742
Middleburg, VA 20118
epilepsytherapy@epilepsytherapy.org
<http://www.epilepsy.com>

Tel: 540-687-8077
Fax: 540-687-8066
Nonprofit corporation that works to advance new treatments for people living with epilepsy. Supports innovative research in academia and industry. Provides information through the www.epilepsy.com website.

Antiepileptic Drug Pregnancy Registry

MGH East, CNY-149, 10th Floor
149 13th Street
Charlestown, MA 02129-2000
info@aedpregnancyregistry.org
<http://www2.massgeneral.org/aed/>

Tel: 888-AED-AED4 (233-2334)
Fax: 617-724-8307
Registry designed to determine what therapies are associated with increased risk of harmful fetal effects. Participation is confidential.

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Glossary

Note: Due to the large number of epilepsy syndromes and treatments, only a few are discussed in this booklet. Additional information may be available from your doctor, other health professionals, medical libraries, or by calling the NINDS Office of Communications and Public Liaison at the number provided on the Information Resources card in the back pocket of this brochure.

absence epilepsy

epilepsy in which the person has repeated absence seizures.

absence seizures

the type of seizure seen in absence epilepsy, in which the person experiences a momentary loss in consciousness. The person may stare into space for several seconds and may have some twitching or jerking of muscles.

ACTH (adrenocorticotrophic hormone)

a substance that can be used to treat infantile spasms.

tonic seizures

seizures which cause a sudden loss of muscle tone, also called *drop attacks*.

auras

unusual sensations or movements that warn of an impending, more severe seizure. These auras are actually simple focal seizures in which the person maintains consciousness.

automatisms

strange, repetitious behaviors that occur during a seizure. Automatisms may include blinks, twitches, mouth movements, or even walking in a circle.

benign infantile encephalopathy

a type of epilepsy syndrome that occurs in infants. It is considered benign because it does not seem to impair cognitive functions or development.

benign neonatal convulsions

a type of epilepsy syndrome in newborns that does not seem to impair cognitive functions or development.

biofeedback

a strategy in which individuals learn to control their own brain waves or other normally involuntary functions. This is an experimental treatment for epilepsy.

celiac disease

an intolerance to wheat gluten in foods that can lead to seizures and other symptoms.

clonic seizures

seizures that cause repeated jerking movements of muscles on both sides of the body.

complex focal seizures

seizures in which only one part of the brain is affected, but the person has a change in or loss of consciousness.

convulsions

sudden contractions of the muscles that may be caused by seizures.

corpus callosotomy

surgery that severs the corpus callosum, or network of neural connections between the right and left hemispheres of the brain.

CT (computed tomography)

a type of brain scan that reveals the structure of the brain.

drop attacks

seizures that cause sudden falls; another term for atonic seizures.

dysplasia

areas of misplaced or abnormally formed neurons in the brain.

early myoclonic encephalopathy

a type of epilepsy syndrome that usually includes neurological and developmental problems.

eclampsia

a life-threatening condition that can develop in pregnant women. Its symptoms include sudden elevations of blood pressure and seizures.

electroencephalogram (EEG)

a test which uses electrodes to record brain waves.

epilepsy syndromes

disorders with a specific set of symptoms that include epilepsy.

excitatory neurotransmitters

nerve signaling chemicals that increase activity in neurons.

febrile seizures

seizures in infants and children that are associated with a high fever.

focal seizures

seizures that occur in just one part of the brain.

frontal lobe epilepsy

a type of epilepsy that originates in the frontal lobe of the brain. It usually involves a cluster of short seizures with a sudden onset and termination.

functional MRI (functional magnetic resonance imaging)

a type of brain scan that can be used to monitor the brain's activity and detect abnormalities in how it works.

GABA (gamma-aminobutyric acid)

an inhibitory neurotransmitter that plays a role in some types of epilepsy.

generalized seizures

seizures that result from abnormal neuronal activity in many parts of the brain. These seizures may cause loss of consciousness, falls, or massive muscle spasms.

glia

cells that regulate concentrations of chemicals that affect neuron signaling and perform other important functions in the brain.

glutamate

an excitatory neurotransmitter that may play a role in some types of epilepsy.

grand mal seizures

an older term for *tonic-clonic seizures*.

hemispheres

the right and left halves of the brain.

hippocampus

a brain structure important for memory and learning.

idiopathic epilepsy

epilepsy with an unknown cause.

infantile spasms

clusters of seizures that usually begin before the age of 6 months. During these seizures the infant may bend and cry out.

inhibitory neurotransmitters

nerve signaling chemicals that decrease activity in neurons.

intractable

about 20 percent of people with epilepsy will continue to experience seizures even with the best available treatment.

ion channels

molecular "gates" that control the flow of ions in and out of cells and regulate neuron signaling.

juvenile myoclonic epilepsy

a type of epilepsy characterized by sudden myoclonic jerks that usually begins in childhood or adolescence.

ketogenic diet

a strict diet rich in fats and low in carbohydrates that causes the body to break down fats instead of carbohydrates to survive.

kindling

a phenomenon in which a small change in neuronal activity, if it is repeated, can eventually lead to full-blown epilepsy.

LaFora's disease

a severe, progressive form of epilepsy that begins in childhood and has been linked to a gene that helps to break down carbohydrates.

Lennox-Gastaut syndrome

a type of epilepsy that begins in childhood and usually causes several different kinds of seizures, including absence seizures.

lesion

damaged or dysfunctional part of the brain or other parts of the body.

lesionectomy

removal of a specific brain lesion.

lobectomy

removal of a lobe of the brain.

magnetic resonance spectroscopy (MRS)

a type of brain scan that can detect abnormalities in the brain's biochemical processes.

magnetoencephalogram (MEG)

a type of brain scan that detects the magnetic signals generated by neurons to allow doctors to monitor brain activity at different points in the brain over time, revealing different brain functions.

metabolized

broken down or otherwise transformed by the body.

monotherapy

treatment with only one antiepileptic drug.

MRI (magnetic resonance imaging)

a type of brain scan that reveals the structure of the brain.

multiple sub-pial transection

a type of operation in which surgeons make a series of cuts in the brain that are designed to prevent seizures from spreading into other parts of the brain while leaving the person's normal abilities intact.

mutation

an abnormality in a gene.

myoclonic seizures

seizures that cause sudden jerks or twitches, especially in the upper body, arms, or legs.

near-infrared spectroscopy

a technique that can detect oxygen levels in brain tissue.

neocortical epilepsy

epilepsy that originates in the brain's cortex, or outer layer. Seizures can be either focal or generalized, and may cause strange sensations, hallucinations, or emotional changes.

neurocysticercosis

a parasitic infection of the brain that can cause seizures.

neurotransmitters

nerve signaling chemicals.

nonconvulsive

any type of seizure that does not include violent muscle contractions.

nonepileptic events

any phenomena that look like seizures but do not result from abnormal brain activity. Nonepileptic events may include psychogenic seizures or symptoms of medical conditions such as sleep disorders, Tourette syndrome, or cardiac arrhythmia.

partial seizures

another term used to describe focal seizures, those that occur in just one part of the brain.

PET (photon emission tomography)

a type of brain scan that can be used to monitor the brain's activity and detect abnormalities in how it works.

petit mal seizures

an older term for *absence seizures*.

photosensitive epilepsy

epilepsy with seizures triggered by flickering or flashing lights. It also may be called photic epilepsy or photogenic epilepsy.

prednisone

a drug that can be used to treat infantile spasms.

progressive epilepsy

epilepsy in which seizures and/or the person's cognitive abilities get worse over time.

progressive myoclonus epilepsy

a type of epilepsy that has been linked to an abnormality in the gene that codes for a protein called cystatin B. This protein regulates enzymes that break down other proteins.

psychogenic seizure

a type of non-epileptic event that is caused by psychological factors.

Rasmussen's encephalitis

a progressive type of epilepsy in which half of the brain shows continual inflammation.

seizure focus

an area of the brain where seizures originate.

seizure threshold

a term that refers to a person's susceptibility to seizures.

seizure triggers

phenomena that trigger seizures in some people. Seizure triggers do not cause epilepsy but can lead to first seizures or cause breakthrough seizures in people who otherwise experience good seizure control with their medication.

simple focal seizures

seizures that affect only one part of the brain. People experiencing simple focal seizures remain conscious but may experience unusual feelings or sensations.

SPECT (single photon emission computed tomography)

a type of brain scan sometimes used to locate seizure foci in the brain.

status epilepticus

a potentially life-threatening condition in which a seizure is abnormally prolonged. Although there is no strict definition for the time at which a seizure turns into status epilepticus, most people agree that any seizure lasting longer than 5 minutes should, for practical purposes, be treated as though it was status epilepticus.

stereotyped

similar every time. In epilepsy this refers to the symptoms an individual person has, and the progression of those symptoms.

sudden unexplained death

death that occurs suddenly for no discernible reason. Epilepsy increases the risk of sudden explained death about two-fold.

temporal lobe epilepsy

the most common epilepsy syndrome with focal seizures.

temporal lobe resection

a type of surgery for temporal lobe epilepsy in which all or part of the affected temporal lobe of the brain is removed.

tonic seizures

seizures that cause stiffening of muscles of the body, generally those in the back, legs, and arms.

tonic-clonic seizures

seizures that cause a mixture of symptoms, including loss of consciousness, stiffening of the body, and repeated jerks of the arms and legs. In the past these seizures were sometimes referred to as *grand mal* seizures.

transcranial magnetic stimulation (TMS)

a procedure which uses a strong magnet held outside the head to influence brain activity. This is an experimental treatment for seizures.

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"Seizures and Epilepsy: Hope Through Research," NINDS. Publication date May 2004.

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